

WHAT IS CLAIMED IS:

1. A method of screening an agent for a pharmacological activity,
comprising:

- 5 (a) providing a multi-well plate, the wells containing teleosts;
(b) introducing agents into different wells of the multi-well plate,
and incubating the agents with the teleosts for sufficient time to induce a response in the
teleosts indicative of the pharmacological activity;
(c) introducing a labelling reagent into each well, which, through
10 processing by or binding to a component of the teleost, generates a detectable signal
dependent on the extent of the response in the teleost;
(d) detecting the signal in each well as an indication of the
pharmacological activity of the agent introduced in the well.

15 2. The method of claim 1, wherein the detectable signal is an
optically detectable signal.

3. The method of claim 1, wherein the detectable signal is detected
using a microplate reader.

20 4. The method of claim 1, wherein the introducing steps are
performed using automated liquid handling apparatus.

5. The method of claim 1, wherein a single teleost occupies in
25 each well.

6. The method of claim 1, wherein a plurality of teleosts occupy
each well.

30 7. The method of claim 1, further comprising distributing teleosts
into wells using a particle dispenser.

8. The method of claim 1, wherein the labelling reagent is a substrate of an enzyme, and the response is an increase or decrease in activity of the enzyme.

5 9. The method of claim 1, wherein the labelling reagent comprises an antibody, and the detectable signal is generated by the antibody bound to a cellular receptor of the teleost.

10 10. The method of claim 9, wherein the antibody is labelled.

11. The method of claim 9, wherein the labelling reagent comprises a first unlabelled antibody and a second labelled antibody that binds to the first antibody.

15 12. The method of claim 1, wherein the response is a change in number of cells or types of cells of the teleost.

20 13. The method of claim 1, wherein the labelling reagent is a nucleic acid, and the detectable signal is generated by the nucleic acid bound to a nucleic acid of the teleost.

25 14. The method of claim 1, further comprising contacting the labelling reagent with a second labelling reagent that binds to the labelling reagent thereby generating the detectable signal.

15. The method of claim 1, further comprising between steps (b) and (c) detecting an optical density within each well to distinguish teleosts that survive incubation with the agent and teleosts that die due to incubation with the agent.

30 16. The method of claim 1, wherein step (c) is performed on a subset of wells containing teleosts that survive incubation with the compound.

17. The method of claim 1, wherein the teleosts are zebrafish.

18. The method of claim 1, wherein the teleosts are embryos, larva or adults.

19. The method of claim 1, wherein the teleosts are synchronized embryos.

20. The method of claim 1, further comprising performing a confirmatory assay on a subset of agents indicated to have the pharmacological activity, the confirmatory assay comprising detecting a second response of the teleosts, the same or different than the response, wherein the second response is a confirmatory indicator of the pharmacological activity.

21. The method of claim 20, wherein the response and the second response are the same, and the detecting step (c) is performed with a plate reader, and the detecting step in the confirmatory assay is performed with a microscope.

22. The method of claim 1, further comprising determining an LD50 on a subset of agents indicated to have pharmacological activity.

23. The method of claim 1, further comprising determining organ-specific toxicity on a subset of agents indicated to have pharmacological activity.

24. The method of claim 1, wherein the pharmacological activity is modulation of angiogenesis, the response is a change in alkaline phosphatase activity of the teleost and the labelling reagent is a substrate for alkaline phosphatase.

25. The method of claim 1, wherein the pharmacological activity is modulation of apoptosis, the response is a change in level of a caspase activity of the teleost and the labelling reagent is a substrate for the caspase.

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26. A method of monitoring distribution of an agent between teleosts and a surrounding medium:

(a) providing a multi-well plate, the wells containing teleosts in a medium, and either the medium or the teleosts or both containing an agent;

(b) culturing the teleosts in the wells;
(c) in each well, determining the amount of the agent in the medium, in the zebrafish or both.

5 27. The method of claim 26, wherein the amount of agent in the medium decreases during step (b) and the method further comprises determining an absorption rate.

10 28. The method of claim 26, wherein the amount of agent in the medium increases during step (b) and the method further comprises determining an excretion rate.

15 29. The method of claim 26, wherein the method further comprises determining a metabolism rate of the agent in the teleost.

30. A method of screening an agent for a property comprising:
(a) providing a multi-well plate, the wells containing teleosts;
(b) introducing agents into different wells of the multi-well plate,
and incubating the agents with the teleosts for sufficient time to induce a response
20 (c) detecting the response in each well as an indication of the property of the agent introduced in the well.